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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/374,721	08/13/1999	JOHN HENRY KENTEN	IGN-2004	4071

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EXAMINER	
ZEMAN, ROBERT A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/374,721	KENTEN ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-87 and 91-116* is/are pending in the application.

4a) Of the above claim(s) *1-81 and 101-116* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *82-87 and 91-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed on 11-17-2004 are acknowledged. Claims 82 and 97-100 have been amended. Claims 1-87 and 91-116 are pending. Claims 1-81 and 101-116 remain withdrawn from consideration. Claims 82-87 and 92-100 are currently under examination.

New Grounds of Rejection

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 82-87 and 91-100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant has amended the claims 82 and 97-100 to recite "ubiquitin fusion protein consisting essentially of endogenous self epitopes". This phrase does not appear in the specification, or original claims as filed. Applicant does not point out specific basis for this limitation in the application, and none is apparent. Moreover, throughout the specification the open "comprising" language is used to describe the claimed ubiquitin fusion proteins. Therefore this limitation is new matter.

Claim Rejections Maintained

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejections of claims 82-87 and 91-100 under 35 U.S.C. 103(a) as being unpatentable over Mouritsen et al. (WO 95/05849) in view of van der Zee et al. (Vaccine Vol. 13, No. 8, pages 753-758, 1995) is maintained for of record.

Applicant argues:

1. The amendment of independent claims 82 and 97-100 to recite "ubiquitin fusion protein consisting essentially of endogenous self epitopes" obviates the rejection.

2.

The motivation for the proposed combination of Mouritsen et al. and van der Zee is lacking.

2. Mouritsen et al. teach the incorporation of one or more T-cell epitopes into the highly conserved self-protein ubiquitin.

3. Mouritsen et al. disclose one ubiquitin fusion protein containing T cell epitopes HEL (50-61) and another containing OVA (325-336).

4. van der Zee et al. teach a fusion protein containing GnRH fused to the T-cell epitope *P. fimbrae.*

5. In both references the foreign epitopes are essential elements of the fusion proteins for generating immune responses.

6. A fusion protein resulting from the combination of ubiquitin and any self-epitopes is neither implicitly nor explicitly suggested.

7. Since the inherent immunogenic property of an ubiquitin fusion protein was not recognized prior to Applicant's discovery, the motivation to combine ubiquitin in a fusion with a self-epitope(s) wherein the ubiquitin is immunogenic for the non-ubiquitin self-epitopes is lacking.

Applicant's arguments have been fully considered and deemed unpersuasive.

The instant invention is drawn to methods for stimulating an immune response in an animal, the immune response being directed to a self-epitope utilizing a ubiquitin fusion protein consisting essentially of endogenous self epitopes the ubiquitin fusion protein comprising ubiquitin fused to one

or more epitope containing segments comprising tow or more identical or non-identical non-ubiquitin self epitopes (either GnRH or growth hormone).

Applicant's argument that the amendment to the claim is sufficient to obviate the aforementioned rejection is not persuasive since Applicant fails to demonstrate how the fusion proteins of the instant claims differs from that outlined in the rejection (i.e. disclosed in the art).

Moreover, Applicant's argument that the recognition of the ability of a fusion protei8n to generate antibodies to ubiquitin is not a disclosure or suggestion that an ubiquitin fusion protein consisting essentially of endogenous self-epitopes is immunogenic is not persuasive. As pointed out by Applicant Mouritsen et al. disclose that their fusion proteins induce an immune response to the "self antigen" as required by the rejected claims.

As outlined previously, Mouritsen et al. disclose the attachment of one or more T cell epitopes into the highly conserved self-protein ubiquitin (see pages 6-7). Mouritsen discloses 2 different ubiquitin fusion proteins: one containing the T-cell epitope ovalbumin (OVA 325-336) and the other containing the T-cell epitope HEL (50-61). Injection of said fusion proteins into mice elicited a strong antibody response to the fusion protein. Moreover, Mouritsen et al. disclose, "the insertion of one **or more** foreign T cell epitopes induces a profound auto-antibody response against said proteins" (see page 6, lines 31-33). Finally, Mouritsen discloses, "the antibody response induced was not necessarily restricted to the inserted T cell epitopes" (see page 6, lines 33-35). van der Zee et al. teach a fusion protein comprising GnRH fused to fimbrae for the development of a contraceptive vaccine for use in domestic animals (see abstract and Figure 4 on page 757). van der Zee et al. also disclose that GnRH is one of the most attractive vaccine components for the immunoneutralization because it is regarded as the key regulatory peptide in the reproduction cycle of mammals (see page

753, column 1). Finally, van der Zee et al. disclose that vaccination of female rats and bull calves with said fusion protein induced not only serological, but also pharmacological effects (see page 757) and as a consequence, that GnRH is a promising candidate for the use in the development of a contraceptive vaccine. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify ubiquitin fusion proteins disclosed by Mouritsen et al. to use GnRH as the self epitope as disclosed by van der Zee et al. since GnRH is considered the pivotal regulatory peptide in mammalian reproduction and there is a demand for an effective, low cost means of controlling fertility in domestic animals. The resulting fusion protein would benefit from the increased stabilization, increased efficiency of translation and increased preservation of biological activity due to proper folding associated with ubiquitin fusion proteins, as well as the increased efficacy of associated with the use of the GnRH self antigen. Moreover, as pointed out by Applicant, the ability of ubiquitin to generate an immune response to a self-epitope is an inherent characteristic of the fusion protein and hence the fusion proteins resulting from the combination of the teachings of Mouritsen et al. and van der Zee et al. would have all the immunological characteristics of the instant invention. The mere recognition of inherent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Thus, although the prior art does not specifically anticipate the claimed functional interactions, it is the combination of the references that would inherently lead to the modification of the immunological properties. Moreover, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re

Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MARK NAVARRO
PRIMARY EXAMINER

Robert A. Zeman
March 7, 2005